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Substitute for (PPT) 449APTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 1

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Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Complete if Known

Application Number 10/091,609
Filing Date March 5, 2002
First Named Inventor Adnan M. M. Mjalli
Group Art Unit 1626
Examiner Name [Signature]
Attorney Docket Number 41305-271622 (2001-07)
Express Mail Certificate EV 032 108 785 US

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
[Signature]	1	3,951,968		Claude P. Fauran et al.	04-20-76	
[Signature]	2	6,316,474		John A. McCauley et al.	11-13-01	

FOREIGN PATENT DOCUMENTS

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		Office ³	Number ⁴	Kind Code ² (if known)				
[Signature]	3	FR	2160719		Fauran	07-06-73		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
[Signature]	4	PCT Notification of Transmittal of the International Search Report corresponding to PCT application from PCT/US02/06706 ("Benzimidazole Derivatives as Therapeutic Agents") June 26, 2002	✓

Examiner
Signature

[Signature]

Date
Considered

8/27/03

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¹ Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.

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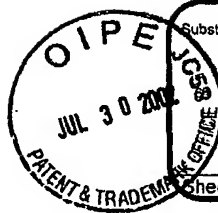
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First Named Inventor Adnan M.M. Mjalli
Group Art Unit 1626
Examiner Name [Redacted]
Attorney Docket Number 41305-271622 (2001-07)
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		Number	Kind Code ² (if known)			
[Signature]	1	4,166,452		Generales, Jr.	09-04-79	
[Signature]	2	4,265,874		Bonsen, et al.	05-05-81	
[Signature]	3	4,356,108		Schwab, et al.	10-26-82	
[Signature]	4	4,873,313		Crawford, et al.	10-10-89	
[Signature]	5	5,202,424		Vlassara, et al.	04-13-93	
[Signature]	6	5,585,344		Vlassara, et al.	12-17-96	
[Signature]	7	5,688,653		Ulrich, et al.	11-18-97	
[Signature]	8	5,864,018		Morser, et al.	01-26-99	
[Signature]	9	5,939,526		Gaugler, et al.	08-17-99	
[Signature]	10	6,100,098		Newkirk	08-08-00	

FOREIGN PATENT DOCUMENTS

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		Office ³	Number ⁴	Kind Code ² (if known)				
[Signature]	11	WO	00/20458		The Trustees of Columbia University in NYC	04-13-00		✓
[Signature]	12	WO	00/20621		The Trustees of Columbia University in NYC	04-13-00		✓
[Signature]	13	WO	97/26913		The Trustees of Columbia University in NYC	07-31-97		✓
[Signature]	14	WO	97/39121		Schering Aktiengesellschaft	10-23-97		✓
[Signature]	15	WO	97/39125		Schering Aktiengesellschaft	10-23-97		✓
[Signature]	16	WO	98/22138		The Trustees of Columbia University in NYC	05-28-98		✓
[Signature]	17	WO	99/07402		The Trustees of Columbia University in NYC	02-18-99		✓
[Signature]	18	WO	99/18987		The Trustees of Columbia University in NYC	04-22-99		✓
[Signature]	19	WO	99/54485		The Trustees of Columbia University in NYC	10-28-99		✓
[Signature]	20	WO	95/09838		Merrell Dow Pharmaceuticals Inc.	04-13-95		✓
[Signature]	21	WO	95/35279		Merrell Pharmaceuticals Inc.	12-28-95		✓
[Signature]	22	WO	97/22618		Vertex Pharma- ceuticals Incorporated	06-26-97		✓
[Signature]	23	WO	96/32385		Hoechst Marion Roussel Inc.	10-17-96		✓
[Signature]	24	WO	99/50230		Vertex Pharma- ceuticals Incorporated	10-07-99		✓

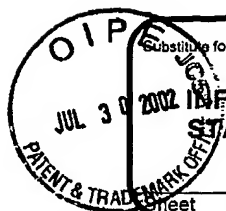
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Sheet 2 of 4

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Application Number	10/091,609
Filing Date	March 5, 2002
First Named Inventor	Adnan M.M. Mjalli
Group Art Unit	1626
Examiner Name	Unassigned Stockton
Attorney Docket Number	41305-271622 (2001-07)
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25	GB	2 005 674	Carlo Erba S.p.A.	04-25-79	✓
26	WO	98/33492	Fox Chase Cancer Center	08-06-98	✓
27	WO	99/25690	University of Kansas Medical Center	05-27-99	✓
29	WO	01/12598	Trustees of Columbia Univ. in NYC	02-22-01	✓

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.†	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
	29	Albercio, F. & Carpino, L.A., "Coupling Reagents and Activation" <i>Methods in Enzymology</i> 289:104-126, Academic Press, San Diego (1997)	✓
	30	Barton, J.W., "In Protection of N-H Bonds and NR ₃ " <i>Protective Groups in Organic Chemistry</i> , J.F.W. McOmie, ED., Plenum Press, New York, NY (1973)	✓
	31	Berge, S.M., et al., "Pharmaceutical Salts" <i>Journal of Pharmaceutical Sciences</i> 66:1-19 (1977)	✓
	32	Chitaley, K., et al., "Antagonism of Rho-Kinase Stimulates Rate Penile Erection via a Nitric Oxide-Independent Pathway" <i>Nature Medicine</i> 7:119-122 (2002)	✓
	33	Degenhardt, T.P., et al., "Chemical Modification of Proteins by Methylglyoxal" <i>Cell Mol. Biol.</i> , 44:1139-1145 (1998)	✓
	34	Dyer, D.G., et al., "Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging" <i>J. Clin. Invest.</i> , 91:2463-2469 (1993)	✓
	35	Dyer, D.G., et al., "Formation of Pentosidine during Nonenzymatic Browning of Proteins by Glucose" <i>J. Biol. Chem.</i> , 266:11654-11660 (1991)	✓
	36	Greene, T.W., "Protection for the Amino Group" <i>Protective Groups in Organic Synthesis</i> , John Wiley and Sons, New York, NY, Chapter 7 (1981)	✓
	37	Hammes, H.P., et al., "Diabetic Retinopathy Risk Correlates with Intracellular Concentrations of the Glycoxidation Product N ^ε -(Carboxymethyl) Lysine Independently of Glycohaemoglobin Concentrations" <i>Diabetologia</i> , 42:603-607 (1999)	✓
	38	Hoffman, M.A., et al., "RAGE Mediates a Novel Proinflammatory Axis: A Central Cell Surface Receptor for S100/Calgranulin Polypeptides" <i>Cell</i> , 97:889-901 (1999)	✓
	39	Hori, O., et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Cellular Binding site for Amphoterin" <i>J. Biol. Chem.</i> , 270:25752-761 (1995)	✓
	40	Huttunen, H.J., et al., "Receptor for Advanced Glycation End Products (RAGE)-Mediated Neurite Outgrowth and Activation of NF-Kappa B Require the Cytoplasmic Domain of the Receptor But Different Downstream Signaling Pathways" <i>J. Biol. Chem.</i> 274(28):19919-24 (1999)	✓
	41	Kumar, S.R., et al., "RAGE at the Blood-Brain Barrier Mediates Neurovascular Dysfunction Caused by Amyloidβ ₁₋₄₀ Peptide" <i>Neurosci. Program</i> , 141-#255.19 (2000)	✓

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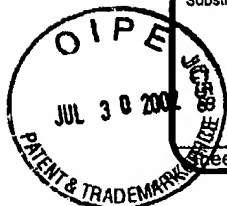
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	42	Leder, A. et al., "v-HA-ras Transgene Abrogates the Initiation Step in Mouse Skin Tumorigenesis: Effects of Phorbol Esters and Retinoic Acid" <i>Proc. Natl. Acad. Sci., USA</i> , 87:9178-9182 (1990)	✓
	43	Li, J. et al., "Sp1-Binding elements in the Promoter of RAG Are Essential for Amphoterin-Mediated Gene Expression in Cultured Neuroblastoma Cells." <i>J. Biol. Chem.</i> , 273:30870-30878 (1998)	✓
	44	Li, J. et al., "Characterization and Functional Analysis of the Promoter of RAGE, the Receptor for Advanced Glycation End Products," <i>J. Biol. Chem.</i> , 272:16498-16506 (1997)	✓
	45	Lugering, N. et al., "The Myeloid Related Protein MRP8/14 (27E10 Antigen)—Usefulness as a Potential Marker for Disease Activity in Ulcerative Colitis and Putative Biological Function" <i>Eur. J. Clin. Invest.</i> , 25:659-664 (1995)	✓
	46	Miyata, T. et al., "β ₂ -Microglobulin Modified with Advanced Glycation End Products Is a Major Component of Hemodialysis-Associated Amyloidosis" <i>J. Clin. Invest.</i> , 92:1243-1252 (1993)	✓
	47	Miyata, T. et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Central Mediator of the Interaction of AGE-β ₂ Microglobulin with Human Mononuclear Phagocytes Via an Oxidant-Sensitive Pathway" <i>J. Clin. Invest.</i> , 98:1088-1094 (1996)	✓
	48	Neeper, M., et al., "Cloning and Expression of a Cell Surface Receptor for Advanced Glycosylation End Products of Proteins" <i>J. Biol. Chem.</i> , 267:14998-15004 (1992)	✓
	49	Parkkinen, J. et al., "Amphoterin, the 30-kDa Protein in a Family of HMG1-Type Polypeptides" <i>J. Biol. Chem.</i> , 268:19726-19738 (1993)	✓
	50	Rammes, A. et al., "Myeloid-Related Protein (MRP) 8 and MRP 14, Calcium-Binding Proteins of the S100 Family, Are Secreted by Activated Monocytes via a Novel, Tubulin-Dependent Pathway" <i>J. Biol. Chem.</i> , 272:9496-9502 (1997)	✓
	51	Rauvala, H. et al., "Isolation and Some Characteristics of an Adhesive Factor of Brain That Enhances Neurite Outgrowth in Central Neurons" <i>J. Biol. Chem.</i> , 262:16625-16635 (1987)	✓
	52	Reddy, S. et al., "N ^ε -(Carboxymethyl) Lysine Is a Dominant Advanced Glycation End Product (AGE) Antigen in Tissue Proteins" <i>Biochem.</i> , 34:10872-10878 (1995)	✓
	53	Schafer, B.W., et al., "The S100 Family of EF-Hand Calcium-Binding Proteins: Functions and Pathology" <i>TIBS</i> , 21:134-140 (1996)	✓
	54	Schleicher, E.D., et al., "Increased Accumulation of the Glycoxidation Product N ^ε -(Carboxymethyl) Lysine in Human Tissues in Diabetes and Aging" <i>J. Clin. Invest.</i> , 99(3):457-468 (1997)	✓
	55	Schmidt, A.M. et al., "The Dark Side of Glucose" <i>Nature Med.</i> , 1:1002-1004 (1995)	✓
	56	Schmidt, A.M., et al., "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) Mediates Binding of AGEs: A Novel Target for Therapy of Diabetic Complications:" <i>Supplement to Circulation</i> Vol. 96, #194 (1997)	✓
	57	Taguchi, A. et al., "Blockade of RAGE—Amphoterin Signalling Suppresses Tumour Growth and Metastases" <i>Nature</i> , 405:354-360 (2000)	✓

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58	Tanaka, N., et al., "The Receptor for Advanced Glycation End Products Is Induced by the Glycation Products Themselves and Tumor Necrosis Factor- α through Nuclear Factor- κ B, and by 17 β -Estradiol through Sp-1 in Human Vascular Endothelial Cells" <i>J. Biol. Chem.</i> , 275:25781-25790 (2000)	✓
59	Teillet et al., "Food Restriction Prevents Advanced Glycation End Product Accumulation and Retards Kidney Aging in Lean Rats" <i>J. Am. Soc. Nephrol.</i> , 11:1488-1497 (2000)	✓
60	Vlassara, H., "Advanced Glycation End-Products and Atherosclerosis" <i>The Finnish Medical Society DUODECIM, Ann. Med.</i> , 28:419-426 (1996)	✓
61	Wautier et al., "Receptor-Mediated Endothelial Cell Dysfunction in Diabetic Vasculopathy: Soluble Receptor for Advanced Glycation End Products Blocks Hyperpermeability in Diabetic Rats" <i>J. Clin. Invest.</i> , 97:238-243 (1996)	✓
62	Yan, S.-D., et al., "RAGE and Amyloid- β Peptide Neurotoxicity in Alzheimer's Disease" <i>Nature</i> 382:685-691 (1996)	✓
63	Yan, S.-D., et al., "An Intracellular Protein That Binds Amyloid- β Peptide and Mediates Neurotoxicity in Alzheimer's Disease" <i>Nature</i> , 389:689-695, (1997)	✓
64	Yan, S.-D. et al., "Amyloid- β Peptide—Receptor for Advanced Glycation Endproduct Interaction Elicits Neuronal Expression of Macrophage-Colony Stimulating Factor: A Proinflammatory Pathway in Alzheimer Disease" <i>Proc. Natl. Acad. Sci., USA</i> , 94:5296-5301 (1997)	✓
65	Yan, S.-D. et al., "Receptor-Dependent Cell Stress and Amyloid Accumulation in Systemic Amyloidosis" <i>Nat. Med.</i> 6:643-651 (2000)	✓
66	Yan, S.-D. et al., "Enhanced Cellular Oxidant Stress by the Interaction of Advanced Glycation Endproducts With Their Receptors Binding Proteins" <i>J. Biol. Chem.</i> 269:9889-9897 (1994)	✓
67	Zimmer, D. et al., The S100 Protein Family: History, Function, and Expression" <i>Brain Res. Bull.</i> 37:417-429 (1995)	✓
68	International Search Report for PCT/US 01/17251 dated 8/14/01	✓

Examiner Signature *Lam J. Stocklin* Date Considered 8/27/03

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